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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/777,425	02/12/2004	Paul R. Sanberg	1372.129.PRC	4329

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EXAMINER	
KIM, TAEYOON	
ART UNIT	PAPER NUMBER
1651	

MAIL DATE	DELIVERY MODE
11/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/777,425	SANBERG ET AL.	
	Examiner	Art Unit	
	Taeyoon Kim	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-12 and 14-26* is/are pending in the application.

4a) Of the above claim(s) *19-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-12 and 14-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Applicant's amendment and response filed on Sept. 27, 2007 has been received and entered into the case.

Claims 2-4 and 13 are canceled, claims 19-26 have been withdrawn from consideration as being drawn to non-elected subject matter. Claims 1, 5-12 and 14-18 have been considered on the merits. All arguments have been fully considered.

The claim rejection under 35 U.S.C.§112 has been withdrawn due to the amendment.

The claim rejection under 35 U.S.C. 102(b) to claims 1 and 11, based on Chen et al. in light of Lim, has been withdrawn due to the amendment.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 6-10, 12 and 14-16 stand rejected under 35 U.S.C. 102(a) as being anticipated by Dengler et al. (Herz, 2002).

Claims 1, 6-10, 12 and 14-16 are drawn to a method of treating myocardial infarction comprising administering an effective amount of a composition comprising a human umbilical cord blood cell to a human patient in need thereof, wherein the

umbilical cord blood cell differentiates into a cardiac muscle (claims 1, 6, 7 and 12); a limitation to the human umbilical cord blood cell being a mesenchymal cell (claims 8 and 16); a limitation to the umbilical cord blood cell being administered directly to heart tissue (claims 9 and 14) or systemically (claims 10 and 15).

Dengler et al. teach a method of treating myocardial infarction by administering umbilical cord stem blood cells directly into the heart tissue or systemically (intravenously) to a human patient in need thereof (see entire document; especially p. 604, right column and Fig. 1 in p.601).

Thus, the reference anticipates the claimed subject matter.

In the response to the previous office action, applicant argued that the reference does not provide any information on the administration of umbilical cord blood cells, the amount of cells needed, or any other information. This argument is not persuasive because Dengler et al. indeed teach information on the administration of umbilical cord blood cells such as systematic administration including intravenous injection (see Fig. 1). The assertion that the reference does not teach the amount of cells and any other information is not persuasive because the claims of interest (i.e. claims 1-4, 6-10 and 12-16) do not claim such limitations. In terms of whether or not the reference enables the method, M.P.E.P. §2121 states that prior art is presumed to be operable/enabling, quoting "When the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. In re Sasse, 629 F.2d 675, 207 USPQ 107 (CCPA 1980).

See also MPEP § 716.07." Therefore, applicant has to provide facts that the reference's teaching is not enabling. The applicant's mere assertion that the reference is not enabling is not sufficient to prove that the reference is not enabling.

Applicant quoted the sentences "... the largest obstacle against ... will be the tissue incompatibility on the level of the HLA system" and "umbilical cord stem cells ... show few differences compared with embryonic stem cells regarding the use for cardiac regeneration" from the reference. Applicant interpreted the sentences as if the disclosure indicates the lack of enablement for the method of the reference. The examiner disagrees with the assertion. The sentences quoted above do not particularly teach that the use of either embryonic stem cells or umbilical cord blood stem cells is not enabling for the treatment of human heart tissue. It is true that it raises an issue of an obstacle in using the stem cells for the cellular therapy, but such an obstacle is well known in the art and can be easily solved by using homologous cells or cells from HLA compatible sources. Therefore, the reference is considered enabling.

Applicant argued that the reference merely name or describe the subject matter. The examiner respectfully disagrees with the assertion because the reference clearly teaches all the limitations claimed in the current invention, and it is not merely naming the subject matter. The reference teaches the use of umbilical cord stem cells in treating human myocardial infarction by administering the cells intravenously or intracoronarily (see Fig. 1).

Applicant argued that the reference does not provide information in carrying out circulatory or cardiac disease treatment. This is not a persuasive argument because

Dengler et al. clearly teach a method to treat infracted heart using stem cells, thus it is about the treatment to circulatory or cardiac disease treatment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 5-12 and 14-18 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Dengler et al. (supra) in view of Broxmeyer (1995; IDS ref) and in further view of Lim et al. (supra), Anversa (US 2002/0061587) and Edelberg et al (US 2003/0091547).

Claims 1, 5-12 and 14-18 are drawn to a method of treating myocardial infarction comprising administering an effective amount of a composition comprising a human umbilical cord blood cell comprising mesenchymal cell to a human patient in need

thereof directly to heart tissue or systemically, wherein the umbilical cord blood cell differentiates into a cardiac muscle; a limitation to the umbilical cord blood cells being administered within approximately 48 hours after the onset of myocardial infarction (claims 5 and 17); a limitation to the umbilical cord blood composition comprising at least about 6 million white blood cells per milliliter of the composition (claims 11 and 18).

Dengler et al. anticipate the limitation of claims 1, 6-10, 12 and 14-16, and therefore render obvious (see above).

Dengler et al. do not teach the presence of at least 6 million white blood cells in the composition comprising umbilical cord blood cells.

Broxmeyer et al. teach the use of umbilical cord blood.

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to replace the umbilical cord blood stem cells of Dengler et al. with the umbilical cord blood, which comprises stem cells/progenitor cells as well as white blood cells according to Lim et al.

The skilled artisan would have been motivated to make such a modification because Dengler et al. disclose various different cells for treatment of myocardial infarction including endothelial progenitor cells (see Table 1), and Edelberg et al. teach the use of endothelial progenitor cells isolated from umbilical cord blood in treatment of myocardial infarction (see paragraph [0018]). Furthermore, Broxmeyer teaches that umbilical cord blood contains hematopoietic stem and progenitor cells (see whole document), and hematopoietic stem cells can be used in treatment of myocardial infarction taught by Anversa (see paragraph [0005]). Since hematopoietic stem cells

and endothelial progenitor cells are used for treatment of myocardial infarction, and it is inherent property of umbilical cord blood contain hematopoietic stem cells and endothelial progenitor cells, a person of ordinary skill in the art would have a motivation to use umbilical cord blood in place of isolated umbilical cord blood stem cells of Dengler et al., and reasonably expect success in using umbilical cord blood.

Although Dengler et al. do not teach the time frame of administration of the cell composition or the presence of at least about 6 million white blood cells in the composition, it would have been obvious for a person of ordinary skill in the art to routinely optimize because the time point when the composition being administered used in the claimed method is a result-effective variable. As such, the variables would be routinely optimized by one of ordinary skill in the art in practicing the invention disclosed by those references. Generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed atl a temperature of 100°C and an acid concentration of 10%.); >see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the

motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); ** In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the :references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Accordingly, the claimed invention was prima facie obvious to one of ordinary skill in the art at the time the invention was made especially in the absence of evidence to the contrary.

In the response to the claim rejection, applicant argued that the references used for the claim rejection are not analogous. This is not persuasive because the references clearly analogous to the current invention related to the treatment of myocardium damage (myocardial infarction) with umbilical cord blood stem cells. Dengler et al. teach a method of using umbilical cord stem cells in treatment of myocardial infarction. Broxmeyer et al. teach the use of umbilical cord blood, which comprises hematopoietic stem and progenitor cells. Lim et al. is related to umbilical cord blood for transplantation. Edelberg et al. teach the use of endothelial progenitor cells from umbilical cord blood in treatment of myocardial infarction. Anversa teaches the use of hematopoietic stem cells in treatment of myocardial infarction. Therefore, all references in the claim rejection are analogous to the current invention.

Applicant argued that a prima facie case must show the obviousness of the current invention, not the obviousness to try. The rejection provided to combine the teaching of Dengler et al. and Broxmeyer et al. with reasonable expectation of success, and further, in regard to the limitations of cell number and the time point when the cells being delivered are considered as result-effective variables, which can be optimized routinely. Thus, a prima facie obviousness was established.

Furthermore, in regard to the applicant's argument that the claim rejection is based on "obviousness to try", the Supreme Court recently states in KSR v. Teleflex (550 US82 USPQ2d 1385, 2007) "The same constricted analysis led the Court of Appeals to conclude, in error, that a patent claim cannot be proved obvious merely by showing that the combination of elements was "obvious to try." Id., at 289 (internal quotation marks omitted). When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103."

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taeyoon Kim whose telephone number is 571-272-9041. The examiner can normally be reached on 9:00 am - 5:00 pm ET (Mon-Thu).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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